

**PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE  
PATENT EXAMINING OPERATION

First Named Inventor: Bandi PARTHASARADHI REDDY

Serial No: 10/510,410

Group Art Unit: 1625

Filed: 10-06-2004

Examiner: CHANG, CELIA C

Att. Docket No.: H1089/20019

Confirmation No.: 8531

For: PREPARATION OF INTERMEDIATES FOR ACETYL CHOLINESTERASE  
INHIBITORS

**PRE-APPEAL BRIEF REQUEST FOR REVIEW**

Mail Stop AF  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

**INTRODUCTORY COMMENTS**

Applicant(s) hereby request(s) review of the Final Rejection in the above-identified application.

No amendments are being filed with this request.

This request is being filed with a Notice of Appeal.

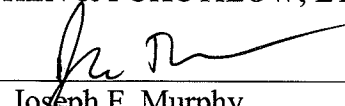
The review is requested for the reason(s) stated on the attached sheet(s) entitled Remarks/Arguments. The Remarks/Arguments section does not exceed five pages in length.

Respectfully submitted,

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July 10, 2008

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Please charge or credit our  
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**REMARKS/ARGUMENTS IN SUPPORT OF THE PRE-APPEAL**  
**BRIEF REQUEST FOR REVIEW**

In response to the Final Office Action dated January 17, 2008, favorable reconsideration is respectfully requested in view of the following remarks. A Notice of Appeal in compliance with 37 C.F.R. 41.31 is filed concurrently herewith.

**ERRORS IN THE EXAMINER'S REJECTION UNDER 35 U.S.C. § 102(b)**

Claims 1-2, 5-6, and 8-10 stand rejected under 35 USC 102(b) over US 4,357,337 (Dubroeuq). This rejection is respectfully traversed.

The Examiner argues that (Office Action at page 2, emphasis added):

Please note that acetic acid can be a solvent when the term solvent is interpreted in the **broadest sense without limitation**. Applicants have calculated that the acetic acid in the prior art is 37 moles, therefore, 0.10 moles serves as catalyst, 36.9-27 moles serves as solvents, and concludes that the amendment did not obviate the anticipation.

**The Standard the Examiner used to interpret the claims is incorrect**

According to the Examiner, the claims were interpreted using the standard wherein the claims were interpreted "in the broadest sense without limitation." This is not the proper standard to use in construing claim language. During patent examination, the pending claims must be "given their broadest reasonable interpretation consistent with the specification." The Federal Circuit's en banc decision in Phillips v. AWH Corp., 415 F.3d 1303, 75 USPQ2d 1321 (Fed. Cir. 2005) expressly recognized that the USPTO employs the "broadest reasonable interpretation" standard. MPEP § 2111.

By improperly construing the "solvent" claim language, the Examiner has failed to consider the actual scope of the claims, and this failure has *undermined* the Examiner's entire claim interpretation and validity analysis. To properly construe the claims, the limitation "solvent" must be considered, using a broadest reasonable interpretation standard. Because the rejections depend upon an improper claim construction, the Examiner's rejections are improper and should be withdrawn

In addition, the '337 Dubroeuq patent discloses a process in which 2-[(4-pyridyl)methyl]-2,3-dihydro-1-1H-indenone (0.269 moles) is hydrogenated at the ambient temperature, under a pressure of 1 bar of hydrogen, in the presence of platinum oxide, in acetic acid solvent (37 moles) to give 2[(4-piperidinyl)methyl]-2,3-dihydro-1-1H-indenone (see '337 patent at column 9, example 4). The '337 patent discloses a method utilizing acetic acid as a solvent, but not as a catalyst (about 37 moles of acetic acid per mole of the 2-[(4-pyridyl)methyl]-2,3-dihydro-1-1H-indenone is used).

However, in contrast, the instantly claimed method utilizes the acid, in the hydrogenation reaction, as a catalyst (0.1 to 10 moles of the acid per mole of the compound of formula II, for example see page 3, ¶[0018] of US 2006/0041140), in a suitable solvent (see page 4, ¶[0033] of US 2006/0041140) using platinum oxide, palladium-carbon, raney nickel or ruthenium oxide catalyst under a hydrogen pressure of 1 to 10 bars. Therefore, the present invention does not use acetic acid as a solvent in the hydrogenation reaction. Thus, the '337 patent does not disclose all the limitations of the claims.

In addition, the Examiner argues that (Office Action at page 2):

Applicants have calculated that the acetic acid in the prior art is 37 moles, therefore, 0.10 moles serves as catalyst, 36.9-27 moles serves as solvents. Thus, the amendment did no obviate the anticipation.

The Examiner is arguing that a portion of the solvent can be considered as solvent, and a portion can be considered as catalyst. Again, this is based on the improper standard the Examiner has used in construing the term "solvent." Under a reasonable interpretation, the same constituent cannot be considered both a solvent and a catalyst.

Accordingly, reconsideration and withdrawal of the rejection of pending claims 1-2, 5-6, and 8-10 under to 35 USC § 102(b) is respectfully requested.

**ERRORS IN THE EXAMINER'S REJECTION UNDER 35 U.S.C. § 102(e)**

Claims 1-3, 5-6, 8-10 stand rejected under 35 USC 102(e) over US 6,649,765 (Vidyadhar). This rejection is respectfully traversed.

The Examiner argues that (Office Action at page 2):

To the extend that the claims read on unlimited solvents and acids, anticipation is maintained. Please note that applicants argument to obviate the prior art is that the

prior art starting material is different as delineated by applicants on page 7 formula A of the response. Please note that the prior art starting material has a "methylene" linker which is not formula A which has a triple bond linker. The prior art anticipated the claims since the claims read on unlimited solvents and acids included those of the prior art.

Again, the Examiner has failed to consider the actual scope of the claims because of the use of an improper standard for claim interpretation, and this failure has undermined the Examiner's entire claim interpretation and validity analysis.

In addition, the instant claims are not drawn to hydrogenation of 5,6-dimethoxy-2-(pyridin-4-yl)-methylene-inda-1-one of formula A of '765 Vidyadhar, but instead are drawn to hydrogenating the compound of formula II, which is clearly a different compound than the formula A compound as set forth in the '765 Vidyadhar patent. The compound of formula II has no double bond in conjugation with a pyridine system, and the claims are directed to a method for synthesis with hydrogen using platinum oxide, palladium-carbon, raney nickel or ruthenium oxide catalyst in the presence of an acid (0.1 to 10 moles of the acid per mole of the compound of formula II, please see page 3, para-0018 of US 2006/0041140) in a suitable solvent (see page 4, ¶[0033] of US 2006/0041140) under a hydrogen pressure of 1 to 10 bars.

In contrast, in the process exemplified in the '765 Vidyadhar patent (see column 3, example 1), 5,6-dimethoxy-2-(pyridin-4-yl)-methylene-inda-1-one (0.035 moles) is hydrogenated with platinum dioxide under 30 psi gauge hydrogen pressure in a solvent mixture containing acetic acid-methanol (200ml:200ml, i.e., about 94 moles of acetic acid per mole of the 5,6-dimethoxy-2-(pyridin-4-yl)-methylene-inda-1-one is used). As can be seen, the instantly claimed method utilizes the acid, in the hydrogenation reaction, as a catalyst in the presence of a suitable solvent (see page 4, ¶[0033] of US 2006/0041140). The instantly claimed method does not use acetic acid as a solvent in the hydrogenation reaction.

Accordingly, reconsideration and withdrawal of the rejection of pending claims 1-3, 5-10, 14 under to 35 USC § 102(e) is respectfully requested.

### **ERRORS IN THE EXAMINER'S REJECTIONS UNDER 35 U.S.C. § 103(b)**

#### **Provisional Rejection under 35 USC 103(a)**

The Examiner argues that even if the compound is as delineated by Applicants' formula

A, claims 1-3, 5-10 and 14 would be rejected under 35 USC 103(a) over '765 Vidyadhar in view of '081 Iimura, and claims 1-3, 5-10 and 14 stand rejected under 35 USC 103(a) over Dubroeuq et al. '337 or Vidyadhar et al. '765 in view of Iimura '081. The rejections are respectfully traversed.

The Examiner argues that (Office Action at page 2, emphasis added):

The compound delineated as formula A on page 7 of the response **would be a precursor for the instant starting material since the triple bonded carbon linker would be hydrogenated**, then the unsaturated carbons of aromatic pyridine will be hydrogenated in a stepwise manner. This rationale is supported by the flow description of Iimura '81 col.6, lines 45-65 wherein functional group other than the pyridinyl ring would be reduced before the aromatic pyridinyl ring is reduced. Per ponderous of evidence in the art supports stepwise reaction (see also Dubroeuq '337 col. 15 preparation (2)). The instant step is a sequence of the prior art continuous process which is prima facie obvious in absence of unexpected results. In re Fong.

However, the instantly claimed method does not use acetic acid as a solvent in the hydrogenation reaction. Both the '337 Dubroeuq patent and '765 Vidyadhar patent discloses the use of acetic acid as a solvent, not as a catalyst. These deficiencies are not cured by the '081 Iimura patent. The '081 Iimura patent discloses a process in which donepezil hydrochloride is prepared by hydrogenating 1-benzyl-4-[(5,6-dimethoxy-1-indanon)-2-yl]methylpyridinium bromide of formula A (see '081 at column 13, example 3) in the presence of platinum oxide catalyst in methanol solvent at room temperature under atmospheric pressure.

The instant claims are not drawn to a method of hydrogenating 1-benzyl-4-[(5,6-dimethoxy-1-indanon)-2-yl]methylpyridinium bromide of formula A of the '081 Iimura patent, but instead hydrogenating the compound of formula II, which is clearly a different compound from the formula A compound of the '081 Iimura patent, which is a quaternary salt. Additionally, as set forth above, the claims are drawn to hydrogenating the compound of formula II, which is clearly a different compound than the formula A compound as set forth in the '765 Vidyadhar patent.

In addition, neither the '765 Vidyadhar nor the '081 Iimura patent teach or suggest the use of acid as a catalyst in the hydrogenation reaction, and this deficiency is not addressed by the

'337 Dubroeuq patent. The '337 patent discloses a method utilizing acetic acid as a solvent, but not as a catalyst. Thus, the instantly claimed methods use different starting materials, have different process steps, and different constituents in the reaction than are taught or suggested in the combination of the '337 Dubroeuq, '765 Vidyadhar and '081 Iimura patents.

The instantly claims are drawn to a method of hydrogenating the compound of formula II with hydrogen using platinum oxide, palladium-carbon, raney nickel or ruthenium oxide catalyst in the presence of an acid (0.1 to 10 moles of the acid per mole of the compound of formula II, please see page 3, para-0018 of US 2006/0041140) in a suitable solvent (please see page 4, ¶[0033] of US 2006/0041140) under a hydrogen pressure of 1 to 10 bars. Furthermore, the '081 patent does not disclose using acid as a catalyst in the hydrogenation reaction. Therefore, all the limitations of the claims are not taught or suggested in the combination of the '337 Dubroeuq, '765 Vidyadhar and '081 Iimura patents.

Accordingly, reconsideration and withdrawal of the rejections of pending claims 1-3, 5-10, 14 under to 35 USC § 103(a) is respectfully requested.

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Accordingly, the Pre-Appeal Brief Conference Panel is respectfully requested to withdraw the appealed rejection(s) and pass this application on to issuance.